

**REMARKS**

Applicants request reconsideration of the above-identified application in view of the following remarks.

Applicants have added new claims 27-29 drawn to methods for identifying an inhibitor of an unphosphorylated JNK3 $\alpha$ . Support for claims 27-29 can be found throughout the specification, for example, on page 18, line 12 to page 21, line 22. New claims 27-29 are not new matter.

**Status of the Claims**

1. List of Pending Claims:

The Examiner indicates that claims 16, 17 and 19-26 are pending in this application with claims 16, 17 and 19-22 withdrawn from consideration as a non-elected invention. Applicants respectfully submit that claims 12-14 should also be pending. Claims 12-14 were originally withdrawn in a September 18, 2003 Amendment and Reply to a December 18, 2002 Office Action, and their status has not been changed since. Applicants therefore request that the record indicate that claims 12-14 are also pending.

Rejoinder:

According to the Examiner, applicants' arguments that withdrawn claims 16, 17 and 19-22 should be rejoined with pending claims 23-26 because a search of designing inhibitors "would likely" turn up references involving identifying inhibitors and vice versa is not persuasive. The Examiner states that the searches are not co-extensive. Thus, claims 16, 17 and 19-22 remain withdrawn.

Applicants traverse. Pending claims 23-26 are drawn to methods for *identifying* an inhibitor of an unphosphorylated JNK3 $\alpha$  molecule. Within said method of identifying an inhibitor, the claims contain the step of "employing said three-dimensional structure to *design* or select a potential inhibitor" (emphasis added; see claim 23, step b and claim 25, step d). Applicants submit that by examining the pending claims and searching the prior art for methods of *identifying* an inhibitor of an unphosphorylated JNK3 $\alpha$ , the Examiner has already searched for methods of *designing* inhibitors of the same. Accordingly, applicants maintain that it would not be burdensome for the Examiner to search for methods of designing and identifying inhibitors of an unphosphorylated JNK3 $\alpha$  since no further search is required.

For the reasons given above, applicants respectfully request that the Examiner reconsider rejoinder of claims 16, 17 and 19-22.

2. Applicants acknowledge with appreciation that rejections under 35 U.S.C. §112, first and second paragraphs, are withdrawn in view of the amendments to claims and applicants arguments.

### The Rejections

#### 35 U.S.C. § 103: Obviousness

Claims 23-26 remain rejected under 35 U.S.C. 103(a) for allegedly being unpatentable over United States patent 6,943,000; effective filing date 10/3/1997 ("Davis").

Claims 23-26 are directed to a method of identifying a JNK3 inhibitor by generating a three-dimensional structure containing coordinates of a specific set of amino acid residues and using said structure to identify the inhibitor while claim 25 requires an additional step of producing a crystal of unphosphorylated JNK3 $\alpha$ . The Examiner contends that Davis is directed to methods of identifying and using JNK3 modulators and that it teaches that computer modeling may be used to identify compounds that modulate JNK3 protein activity

by reacting, for example, with its active site. The Examiner also contends that the JNK3 active site can be identified using methods known in the art including X-ray crystallographic methods. The Examiner further contends that once the three dimensional structure of the JNK3 active site has been determined, candidate modulating compounds which match the active site structure, fit into the active site or interact with groups defining the active site, can be identified.

In addition, the Examiner contends that the activity of the identified ligands is tested and that the method disclosed in Davis is applicable to any known JNK3 proteins or fragments thereof. The Examiner notes that the JNK3 proteins of SEQ ID Nos. 5 and 8 comprise the instantly claimed residues and that SEQ ID No. 10 is a JNK3 fragment truncated at N-terminal. Even though the method disclosed by Davis does not specify the atomic coordinates according to Figure 1A, the Examiner contends that Davis addresses JNK3 proteins having the same sequence. The Examiner additionally contends that while Davis "requires use of the entire JNK3 $\alpha$  protein rather than a specific set of amino acid coordinates, using coordinates of residues of the entire protein would thus include use of residues recited in the claims".

With respect to the specific limitations of atomic coordinates in this instant case, the Examiner contends that they do not distinguish the invention in terms of patentability because they constitute descriptive nonfunctional subject matter as the atomic coordinates in Figure 1A are merely stored so as to be read or outputted by a computer without creating any functional interrelationship. The Examiner maintains that a list of coordinates, as in Figure 1A, represents non-functional descriptive material and does not impart functionality either to the data or to the computer.

The Examiner also contends that Davis is silent with regards to the phosphorylation status of the protein and that there is no reason to believe that the reference requires phosphorylated JNK3 $\alpha$ .

Applicants traverse. Regardless of the disclosure in Davis and the Examiner's contention that coordinates are non-functional descriptive matter, applicants maintain two arguments made earlier.

Davis states only that "the three-dimensional structure of the active site can be determined...using known methods, including X-ray crystallography, which can be used to determine a complete molecular structure..." (emphasis added)

and that computer-based modeling can also be used to complete an incomplete or inaccurate structure. However, the statements in Davis do not meet the requirements for obviousness.

A prima facie showing of obviousness requires some reasonable expectation of success and a teaching or suggestion of all the claim limitations. It is well recognized in the art that there exists is a high degree of unpredictability when crystallizing a protein, solving the structure of a protein, or establishing the active binding site on a protein. In addition, a large amount of experimentation is needed to perform any of the above three steps. Davis, however, merely suggests that a structure of the active site can be determined. Thus, in light of the high degree of unpredictability and the large amount of experimentation required, *there is no reasonable expectation of success.*

Second, Davis does not include all the claim limitations of claims 25 and 26. Davis does not teach or suggest with reasonable expectation of success the steps of producing a crystal of an unphosphorylated JNK3 and determining the three-dimensional atomic coordinates. To the contrary, claims 25 and 26 of the present invention recite

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these steps. Thus, Davis does not render the instant claims obvious.

For at least the reasons given above, applicants respectfully request that the Examiner withdraw the outstanding 35 U.S.C. § 103 rejection.

#### CONCLUSION

Applicants respectfully request that the Examiner reconsider and withdraw all outstanding objections and rejections, enter the amendments, and pass the resulting claims to allowance. Should the Examiner feel that a telephone conference with applicants' representatives would assist the Examiner, he is invited to telephone the undersigned at anytime.

Respectfully submitted,



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